

Imaging of CTLA4 blockade-induced cell replication with (18)F-FLT PET in patients with advanced melanoma treated with tremelimumab.

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Public Summary:

Preclinical models predict that blockade of the coinhibitory molecule cytotoxic T lymphocyte-associated antigen 4 (CTLA4) on lymphocytes results in the release of a cell cycle inhibitory checkpoint, allowing lymphocyte proliferation, tumor targeting, and tumor regression. However, there is a paucity of data demonstrating that lymphocyte proliferation does occur in humans treated with CTLA4-blocking antibodies. **METHODS:** We performed whole-body molecular imaging in patients with advanced melanoma receiving the CTLA4-blocking antibody tremelimumab, allowing the analysis of changes in glucose metabolism using the PET probe (18)F-FDG and cell replication with the PET probe 3'-deoxy-3'-(18)F-fluorothymidine ((18)F-FLT). Cancer cells generally are more metabolically active than non-cancer cells. (18)F-FDG allows us to visualize metabolically active cells, thereby visualizing the cancer. (18)F-FLT allows us to visualize actively dividing cells, thus proliferating lymphocytes can be assessed. **RESULTS:** PET/CT scans obtained at a median of 2 months after initial dosing did not demonstrate significant changes in lesion size or (18)F-FDG or (18)F-FLT uptake when focusing on metastatic lesions. Similarly, there was no difference in (18)F-FDG uptake in the non-melanoma-involved spleen. However, there were significant increases in standardized uptake values for (18)F-FLT in the spleen using post- and pretremelimumab treatment scans. **CONCLUSION:** Molecular imaging with the PET probe (18)F-FLT allows mapping and noninvasive imaging of cell proliferation in secondary lymphoid organs after CTLA4 blockade in patients with metastatic melanoma suggesting that lymphocyte proliferation does occur in humans following treatment with CTLA4-blocking antibodies.

Scientific Abstract:

Preclinical models predict that blockade of the coinhibitory molecule cytotoxic T lymphocyte-associated antigen 4 (CTLA4) on lymphocytes results in the release of a cell cycle inhibitory checkpoint, allowing lymphocyte proliferation, tumor targeting, and regression. However, there is a paucity of data demonstrating that lymphocyte proliferation does occur in humans treated with CTLA4-blocking antibodies. **METHODS:** We tested the role of whole-body molecular imaging in patients with advanced melanoma receiving the CTLA4-blocking antibody tremelimumab, allowing the analysis of changes in glucose metabolism using the PET probe (18)F-FDG and cell replication with the PET probe 3'-deoxy-3'-(18)F-fluorothymidine ((18)F-FLT). **RESULTS:** PET/CT scans obtained at a median of 2 mo after initial dosing did not demonstrate significant changes in lesion size or (18)F-FDG or (18)F-FLT uptake when focusing on metastatic lesions. Similarly, there was no difference in (18)F-FDG uptake in the non-melanoma-involved spleen. However, there were significant increases in standardized uptake values for (18)F-FLT in the spleen using post- and pretremelimumab treatment scans. **CONCLUSION:** Molecular imaging with the PET probe (18)F-FLT allows mapping and noninvasive imaging of cell proliferation in secondary lymphoid organs after CTLA4 blockade in patients with metastatic melanoma.

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